

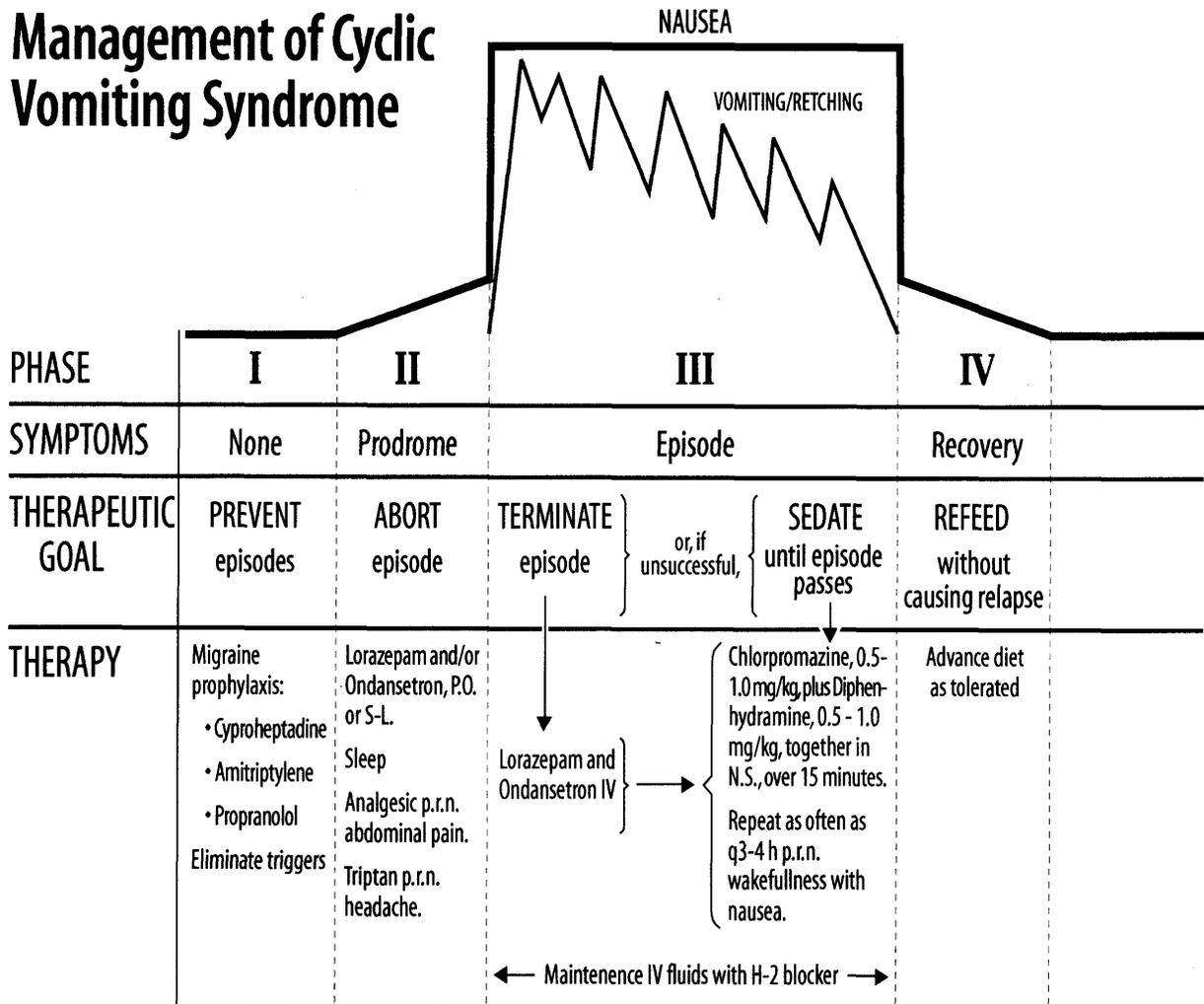
EMPIRIC GUIDELINES FOR TREATMENT OF CYCLIC VOMITING SYNDROME

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There is, as yet, no standard, evidence-based treatment regimen for CVS. Management must be individualized and “fine-tuned” during the course of the patient’s illness. The following guidelines are offered as a conceptual framework from which to begin.

Management strategy is based on the four phases of CVS. Treatment is applied according to the phase the patient is in at the time of presentation.

Management of Cyclic Vomiting Syndrome



PHASE I is the nausea-free *interval between episodes*. Appropriate treatment includes migraine prophylaxis if episodes are frequent, long or difficult to abort; TCA's, propranolol, or cyproheptadine may lessen the frequency of CVS episodes as well as migraine headaches. In addition, try to identify and ameliorate conditions that may predispose to or trigger episodes, such as reflux esophagitis, chronic sinusitis, clinically significant anxiety, PMS, motion sickness, sleep deficits or metabolic stress (e.g. prolonged caloric deprivation in patients who may have a defect in mitochondrial energy production).

PHASE II, the prodrome: This phase starts when the patient begins to feel symptoms signaling the approach of an episode, but is still able to retain oral medications. It ends when either the vomiting phase is successfully aborted or the vomiting begins. The prodrome might last days, minutes, or may not occur at all in patients who wake from sleep already vomiting. To treat it, discern its constituent symptoms and relieve each as quickly as possible, before the prodromal phase gives way to vomiting. For nausea, try ondansetron (Zofran) liquid, tablets or ODT's (oral disintegrating tablets) at 0.3 – 0.4 mg/Kg/dose. (This is twice the dose recommended for chemotherapy patients.) Zofran is non-sedating and safe. Promethazine (Phenergan) may also be effective; it causes sedation, which may or may not be desirable, depending on the patient's circumstances.

Anxiety potentiates nausea. Lorazepam (Ativan) is anxiolytic, anti-emetic and promotes sleep. It works well together with ondansetron. Lorazepam tablets are almost tasteless and can be chewed or dissolved in the mouth without the patient having to drink. In many anxious adult patients, episodes may be triggered by panic attacks. Their prodromal symptoms typically include chills and/or hot flushes, abdominal pain, sweating, trembling, palpitations, pounding heart, dyspnea, light headedness. Alprazolam (Xanax), a rapidly acting anxiolytic, 1 to 2 mg p.o. taken immediately, may relieve panic and abort the vomiting phase.

For midline or high-epigastric *pain* (the predominant symptom in abdominal migraine), try ibuprofen. Dilaudid (hydromorphone) is powerfully anxiolytic as well as analgesic. If abdominal pain is being caused by panic, Dilaudid, p.o. or by suppository, usually relieves nausea and pain when they are symptoms caused by panic. Although nausea is a common side effect of opiates, by contrast, nausea caused by panic is almost always relieved by Dilaudid.

For *headache* with features of common or classical migraine, try ibuprofen, ketorolac or a triptan (by tablet or nasal spray). However, unlike their efficacy in migraine headache, triptans seldom prevent or relieve the abdominal pain or nausea of a CVS attack

A proton pump inhibitor (e.g. Prilosec or Prevacid) may lessen *epigastric distress and heartburn*. (They are useful during the inter-episodic phase in patients with dyspeptic nausea or heartburn.)

Some patients experience *loose stooling*, a symptom that precludes use of suppositories. In most cases, diarrhea is not especially troublesome.

Hypertension and tachycardia, caused by a stress-induced hyper-adrenergic state, may begin during the prodrome and persist throughout the episode. Serious hypertension, if it occurs, may be treated with adrenergic antagonists, e.g., propranolol.

PHASE III: THE VOMITING PHASE is characterized by intense nausea and vomiting. Patients may show behavioral states, such as: 1) subdued, but responsive; 2) an immobile, unresponsive state referred to as "conscious coma"; or 3) writhing and moaning. Patients who are subdued but responsive usually prefer to lie

down, but may be able to move about, watch TV or attempt to play between bouts of vomiting. Patients in “conscious coma” lay motionless, eyes closed, and are so unresponsive that it is difficult to know whether they are awake or asleep. Patients who writhe and moan between bouts of vomiting have intense abdominal ache and/or severe retrosternal pain. Cognition is impaired and the patient is too uncomfortable to give much of a history.

The possible acute complications of untreated episodes include hypovolemic shock, electrolyte depletion, tetany, hematemesis, and secretion of inappropriate anti-diuretic hormone (SIADH). The nausea of CVS episodes is agonizing. Therefore, treatment of CVS episodes must be prompt. If treatment is delayed, the patient’s extreme distress predisposes them to fear the next episode, and, since anticipatory anxiety can cause nausea, their fear may cause more frequent episodes and a coalescent pattern of attacks. Episodes that cannot be aborted should be treated without delay, ideally within an hour of onset. “Watchful waiting” or long waits in treatment facilities are counter-therapeutic.

To treat Phase III, cannulate a vein, draw a baseline CBC, metabolic panel, and whatever diagnostic blood samples are necessary, consider the need for a saline bolus, and then start maintenance IV fluids. Maintenance IV fluids should contain 10% glucose during the first 12 – 24 hours because an episode of vomiting caused by a congenital defect in mitochondrial function (such as *medium chain Acyl Co-A dehydrogenase deficiency (MCAD)*) can mimic CVS. If IV glucose alone is followed by dramatic improvement, a metabolic diagnosis should be pursued. The response or lack of response to IV glucose has diagnostic and therapeutic implications. Otherwise, 5% dextrose in 0.5 N saline with KCl and an H-2 blocker or PPI can be used for IV fluid maintenance.

As soon as IV access is established, attempt to *terminate* the episode by giving lorazepam by slow IV push and ondansetron (0.3-0.4 mg/Kg/dose) by IV piggyback over 15 minutes. The patient will respond in one of three ways: 1) the nausea clears and doesn’t return; 2) the nausea clears, but returns within minutes or hours; or 3) the nausea doesn’t clear.

In the first case, cap or remove the IV, give 4 to 8 mg of ondansetron p.o., demonstrate that the patient can take food or drink without causing a relapse of nausea and send the patient home. In the second and third cases, termination has failed and there is no way to give relief other than to *sedate* the patient. The brain, not the GI tract, is the origin of cyclic vomiting and sleep stops such vomiting. It also makes patients unaware of their nausea, giving them an escape from what would otherwise be relentless misery. Preferred sedative drugs are non-addictive and non-emetogenic. Chlorpromazine combined with diphenhydramine work well: mix chlorpromazine (0.5 – 1 mg/Kg/dose) with diphenhydramine (0.5 – 1 mg/Kg/dose) in 50 cc of normal saline and infuse over 15 minutes. This combination of sedatives should be repeated as needed for wakefulness with nausea, as often as q 3 hours, for as long as the episode lasts. Sedation may be needed for several days, depending on the length of the patient’s episodes and his/her responses to sedation. (Never give Thorazine & Benadryl if the patient is hypotensive or while the patient is sleeping soundly.) Close observation allows for prompt re-administration of the sedative infusion as soon as the patient wakes up in distress.

Keep the patient’s room darkened and quiet. Minimize waking the patient for vital signs and other procedures as much as possible. Try to confine checks of vital signs to the brief intervals of wakefulness between successive sedative infusions.

If the patient does not remain asleep for at least 3 hours at a time, either increase the dose of IV chlorpromazine in the direction of the 1 mg/Kg/dose or give the patient a spot dose of IV lorazepam (0.05 – 0.1 mg/Kg/dose, up to 2-3mg, by slow IV push. Reliance on lorazepam alone for sedation, or too frequent administration of it, causes impairment of memory and alertness, a state that may prolong recovery by a day or two. Chlorpromazine and diphenhydramine don't seem to cause as much "hangover."

Concerned parents understandably feel the need to evoke a response from their sick, uncommunicative child and may repeatedly ask, "Are you OK?" Although children need to know that their parents are available and supportive, they feel burdened by such demands for responsiveness. Family and hospital personnel should avoid causing this kind of distress as much as possible.

Hematemesis is common. It is often due to "prolapse gastropathy" in which there is bleeding of the mucosa of the proximal stomach as intense retching forces the cardia up into the lower esophagus where it is squeezed and bruised. Although hematemesis of this type seldom causes serious blood loss, it does not preclude significant blood loss from the esophageal mucosa or a Mallory-Weiss tear.

Monitor the pH of vomitus. If it remains below 4.5, increase the IV dose of H-2 blocker or PPI.

Intense nausea may be accompanied by SIADH. Monitor urine specific gravity; if it remains high in the presence of adequate hydration, check for low serum osmolality and hyponatremia and restrict water input until lab values return to normal.

Many patients experience intense thirst that compels them to drink, even though they know that the ingested water will come back up almost immediately. If compulsive drinking is followed by self-induced vomiting during episodes, don't mistake this behavior for bulimia! Drinking dilutes acid and bile, thereby making the vomitus less of a contact irritant to the esophagus and mouth. Emesis can be induced more easily from a full stomach than from an empty stomach. The transient lessening of nausea that follows self-induced vomiting makes this comfort-seeking behavior worth the trouble for some patients. Keeping the patient n.p.o. is almost impossible. Sedation eliminates the drink-and-vomit behavior.

Intense nausea may cause patients to spit-out, rather than swallow their saliva. They may carry a pan or towel in which to expectorate. Others are prevented from speaking by a mouthful of saliva they are unwilling to swallow. Patients who are normally appreciative and cooperative when well may become irritable, verbally abusive and demanding during the throes of CVS episodes. Sedation eliminates these behaviors by relieving their distress.

Neutrophilia is sometimes present during attacks, even in the absence of infection. It is probably caused by stress-induced demargination. It, together with abdominal pain and vomiting, can mimic appendicitis or pyelonephritis. Occasionally, increased serum amylase, possibly of salivary origin, mimics pancreatitis.

PHASE IV. The *recovery phase* begins when vomiting and retching cease and the nausea subsides. It ends when the patient's appetite, tolerance for food, and vigor return to normal. Recovery tends to be prolonged when inadequate management of the episode permitted severe fluid and electrolyte deficits and marked weight loss.

Some patients are able to tolerate a regular diet as soon as their nausea lifts. Others may suffer a resumption of nausea and vomiting if they take more than clear liquids initially. It doesn't take long for patients to learn when and what they can eat and drink. Allow them to decide.

Prophylactic medications should be resumed as soon as recovery is complete.

CVS patients and their families have many fears concerning their mysterious, unpredictable disorder. One fear is that the illness might never go away. They need to be assured that, although there may be several or several hundreds of episodes during a course lasting months or decades, CVS, effectively managed, resolves in most cases.

Another fear is that their physician might lose interest and become less accessible. Physicians want to help patients and it is understandable if they become discouraged when they feel unable to help the patient who is not improving. If the physician does lose interest because the challenge seems so daunting, he or she may deprive the patient of what is most essential and most valued under the circumstances: continuation of a relationship with a physician who is caring, accessible and willing to collaborate with them in their struggle for well-being.

Until the time when CVS becomes curable, we must not allow ourselves to be defeated by failure.

David R. Fleisher, MD
Associate Professor, Department of Child Health
University of Missouri
School of Medicine
Columbia, Missouri, USA

fleisherd@health.missouri.edu

www.ch.missouri.edu/fleisher